Splenectomy in Blood Dyscrasia

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• **The decision for splenectomy must be based on a knowledge of the three functions of the spleen: Hematopoiesis (usually ceasing during fetal life but sometimes resuming when bone marrow function fails); filtration of abnormal and senescent cells and control of bone marrow activity, most probably humoral.**

When bone marrow function fails, splenectomy is contraindicated since splenic hematopoiesis becomes a vital function. On the other hand, when a large proportion of erythrocytes are abnormally shaped (spherocytes), although otherwise adequate, the spleen may trap these cells in its filter and destroy large numbers. Splenectomy is beneficial in almost every case of congenital spherocytosis, but in only half the cases of the acquired defect.

In panhematocytopenia, thrombocytopenia and neutropenia, all apparently due to depression of hematopoiesis by endocrine or other action of the spleen, splenectomy may be beneficial if medical therapy fails.

A surgeon undertaking splenectomy should recognize two special problems: (1) The presence of accessory spleens, which if not removed may negate the effects of the operation, and (2) the apparently high rate of infection in infants and children who have undergone splenectomy.

"THE SURGEON is often placed in a somewhat delicate position when asked to see a patient about splenectomy, unless the indications are clear and well-established, as in familial hemolytic anemia. By the time the surgeon's opinion is asked, the physician, in collusion with the hematologist, has already probably decided the issue. The surgeon may thus find himself relegated to the humble position of the craftsman, for he cannot hope to master the intricacies of hematology to an extent which will qualify him to argue on equal terms with those whose business it is to be expert in this branch of medicine. He should be able, however, to make some contribution in the light of his experience with splenectomy and particularly of surgery in general."[6]

This quotation from Edwards challenges surgeons to familiarize themselves with the indications for and the sequelae of splenectomy.

Unlike those diseases in which a certain diagnosis is an indication for a specific treatment, splenic disease is still identified symptomatically, and splenectomy often must be used in the hope of symptomatic relief, rather than in the certainty of relieving an underlying disease. Nevertheless, the surgeon should know which splenic functions he may alter or obliterature by splenectomy.

The first function of the spleen is hematopoiesis, which normally is present only during fetal life. In later life, though, if bone marrow is replaced by tumor, fibrosis or cortical bone tissue, so that normal hematopoiesis becomes impossible, the spleen reverts to its fetal function and becomes a source of formed blood elements. In this condition, known as myeloid metaplasia, splenectomy is contraindicated.

The second function is that of eliminating erythrocytes from the circulation, apparently by filtration. It is not clear how the normal senescent cell is affected by the spleen, since the life span of the erythrocyte (about 120 days[1]) is not prolonged after splenectomy.[15] More definite is the evidence in such blood dyscrasias as congenital spherocytosis. In patients with this disease who receive normal blood, the abnormal spherocytes are found in the spleen in far greater concentration than in the peripheral circulation. Conversely, if spherocytic blood is perfused through an essentially normal spleen (removed from a patient with thrombocytopenic purpura), the abnormal spherocytes are sequestered by the spleen. These findings demonstrate that the spleen does retain morphologically abnormal erythrocytes.

The third function of the spleen is to control bone marrow activity. Since depression of marrow function is relieved after splenectomy, it seems most likely that the spleen produces a hormone that has this depressing effect.

INDICATIONS FOR SPLENECTOMY

Hemolytic Anemia

Congenital hemolytic anemia has a number of descriptive names among which are: Hereditary spherocytosis, congenital hemolytic jaundice, familial hemolytic jaundice, acholuric jaundice, congenital hemolytic anemia, familial hemolytic anemia and spherocytic or globe-cell anemia. The spherocytic tendency is inherited as a Mendelian dominant and is characterized by abnormally thick red blood

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cells. These spherocytes are functionally adequate as to oxygen-carrying capacity, but their abnormal fragility and shape make them ever a prey to the splenic filter.[20,21] Splenectomy therefore both theoretically and in actual practice is a consistently beneficial therapeutic measure and good results can be expected in almost all cases in which diagnosis is clear-cut.

Splenectomy should be performed between acute hemolytic episodes, since operation is much better tolerated if the patient is relatively asymptomatic. This can usually be accomplished either by waiting or by the use of corticotropin (ACTH) or cortisone, and "emergency" splenectomy for congenital hemolytic anemia is rarely necessary.

Acquired hemolytic anemias may be divided into idiopathic and secondary. In the idiopathic acquired as well as in some of the secondary acquired types, the basic defect is a circulating antibody which causes spherocytosis with increased mechanical and osmotic fragility, resulting in hemolytic crises. The condition of the blood may thus appear superficially the same as in congenital hemolytic anemia, particularly during periods of hemolysis. The differential diagnosis is dependent upon two factors. One is the absence of familial incidence and the other is the presence of a circulating antibody which periodically attacks the red cells, causing excessive hemolysis secondary to abnormal shape and increased fragility. Between hemolytic crises, the red cell shape and fragility may be normal even though the antibody is still present. This antibody may be demonstrated in a large proportion of these cases by the Coombs test.[2]

Splenectomy benefits approximately 50 per cent of patients with idiopathic acquired hemolytic anemia, but predicting which will be benefited is quite difficult. If a patient is having serious symptoms, splenectomy should be offered if medical therapy, including use of corticotropin (ACTH) or cortisone, fails.[4]

The chief diagnostic differences between hereditary and acquired spherocytoses are summarized in Table 1.

The secondary acquired hemolytic anemias may be due to splenic involvement from lymphoma, leukemia, Hodgkin's disease, sarcoidosis, Gaucher's disease, kala-azar or tuberculosis. If the hemolytic anemia associated with any of these diseases is of prime importance and does not respond to medical measures, splenectomy may be of some benefit. It should be emphasized, however, that this is symptomatic therapy for hemolytic anemia and not a therapeutic measure for the underlying disease. The cause of this form of hemolysis is uncertain. It is postulated that in some cases in which the spleen becomes greatly enlarged, the organ elaborates a lytic substance which acts on the large amount of blood confined in it.

TABLE 1.—*Findings in Hereditary and Acquired Spherocytosis*[5]

	Hereditary	Idiopathic Acquired
Family history of disease	Usually present	None
Finding of disease in studies of family	Definitely positive	Negative
Abnormal antibody at body temperature	Negative	Positive
Result of Coombs test	Negative	Positive
Survival of transfused erythrocytes	Normal	Reduced

Thrombocytopenia

The basic defect in idiopathic thrombocytopenic purpura is arrest in maturation of the megakaryocyte which is the stem cell of the thrombocyte or platelet. The megakaryocyte fails to form the "buds" which in turn form the platelet.[14] In the majority of patients with idiopathic thrombocytopenic purpura, splenectomy is not necessary for amelioration of the symptoms. Most of the episodes either are self-limited or can be successfully treated with corticotropin or cortisone.[8] However, in some cases there is no response to conservative therapy, whereas 65 to 75 per cent of adults and 90 per cent of children respond well to splenectomy. After splenectomy, the megakaryocytes mature and form buds, and the platelet count increases. Simultaneously, the bleeding tendencies cease. There are observers who still maintain that the spleen acts as a filter of the thrombocyte in this disease; however, most of the evidence points to a humoral substance which arrests maturation of megakaryocytes by depressing bone marrow.

The diagnosis of idiopathic thrombocytopenic purpura usually is not very difficult, but secondary causes of thrombocytopenia must be excluded.[10,11] The essential diagnostic features of idiopathic thrombocytopenic purpura are a history of excessive bleeding or easy bruising, a platelet count of less than 100,000 per cu. mm. of blood, evidence of arrest in maturation of megakaryocytes, an absence of signs of bone marrow involvement by lymphoma, leukemia, or carcinoma, and a similar absence of systemic disease as determined by microscopic examination of peripheral blood. In the majority of cases, the spleen is not palpable in this disease. This finding alone will usually differentiate primary from secondary thrombocytopenia.

In general, secondary thrombocytopenia is a contraindication to splenectomy since it is part of the

systemic disease and splenectomy will be of no benefit. However, when excessive bleeding is a part of the systemic disease and cannot be controlled by the use of corticotropin or cortisone, splenectomy may be recommended and in some instances has controlled the bleeding and given the patient a more comfortable existence for the remainder of his life.

Hypersplenism and Cytopenia

The hypersplenic state may manifest itself through a reduction in all the formed blood elements (panhematocytopenia) or of any of these elements. An important although relatively infrequent deficiency is that of neutrophils (splenic neutropenia). Some investigators attribute this to active depression of bone marrow function such as occurs in idiopathic thrombocytopenic purpura; others believe it may be due to excessive phagocytosis by the spleen. Whatever the cause, splenectomy does result in an increase in leukocytes and freedom from infections secondary to neutropenia. The disease occurs most commonly in women 30 to 60 years old, who become chronically ill with recurrent skin and mouth infections. The spleen is enlarged and leukocytes number 1,000 to 2,000 cells per cu. mm. of blood. The bone marrow is excessively cellular, with many granular cells present although mature forms may be rare. In conjunction with this state, rheumatoid arthritis may be present (Felty's syndrome), but if splenectomy is recommended it should be for the leukopenia alone and not for the arthritis, on which it has no effect.

As previously stated, if all the formed blood elements are deficient, the syndrome is known as panhematocytopenia. In some cases, this may take the form of excessive destruction of blood, the symptoms being those of hemolytic anemia. In others, the deficiency seems to be due to depression of marrow function. As in other hypersplenic syndromes, the condition may be primary—and this responds well to splenectomy—or secondary, as a result of splenic involvement from lymphomas, Gaucher's disease, kala-azar or tuberculosis. The secondary state is less likely to respond to splenectomy, except in isolated instances when symptoms are due to size and malfunction of the spleen.[13]

ACCESSORY SPLEENS

One or more accessory spleens have been found in from 25 to 50 per cent of patients undergoing splenectomy. The possibility of this condition should be at least recognized by the surgeon.[3] Some investigators believe that accessory spleens may not be important; but the consensus is that they may cause the disease process to continue or recur, and therefore should be removed.[12,19]

Three out of four accessory spleens are found in the hilar or pedicle area of the spleen. These present no problem in visualization and removal. More troublesome are the minority found in locations which may seem puzzling until the embryonic development of the spleen is considered. In the twelfth week after conception, the spleen is a differentiated structure situated between the mesonephric and the urogenital folds. During the caudal migration of the genital gland, splenic tissue may be carried along, to be deposited at the upper pole of the left testis and epididymis, or, in females in the region of the left mesosalpinx and mesovarium. The path of migration is in some cases evident in a band of fibrous or splenic tissue, or both, connecting the normal spleen with the ecotopic tissue in the scrotum or the broad ligament. Before splenectomy, the scrotum should be carefully examined in males; in females the entire abdomen including the left adnexa should be searched for accessory spleens. If the postoperative result is not satisfactory, the possibility of accessory spleens should be considered.

SEQUELAE

Most reports on splenectomy make no reference to any untoward sequelae. Some investigators believe that at a given degree of platelet surplus, heparin or some other anticoagulant should be given to obviate thromboembolic disease, but others consider this precaution unnecessary. Since it is known that if all the other clotting elements in the blood are normal an increase in platelets increases coagulation, it seems reasonable that any increased danger should be met by antithrombotic measures.

In recent years there has been an increase in reports of infections in children following splenectomy. In 1952 King and Shumacker[9] reported case histories of five infants under six months of age who had multiple infections following splenectomy. The indication for splenectomy in all these infants was congenital hemolytic anemia. Four of the five infants had either meningitis or overwhelming meningococcemia in from six weeks to three years after operation, and one of the four died of the infection. The fifth child was returned to the hospital a few days after discharge following splenectomy with a rapidly fatal febrile illness, apparently infectious in nature. In 1955, though, Walter and Chaffin[18] reported on ten infants from the Children's Hospital in Los Angeles who had had splenectomy below the age of 7 months; in this group there was no increase in the infection rate. At the Children's Hospital in Boston an increased incidence of pneumococcic infections in infants occurred following splenectomy, and a similar observation was made by Smith in New

York.[16] The cause of this increased rate of infections is not clear, especially since it has been shown that the gamma globulin fraction is not decreased in infants after splenectomy. Nevertheless, children should be observed closely for infections after splenectomy so that therapy can be instituted at an early date if there is any indication of infectious disease.

There appears to be no increase in infections in adults following splenectomy.

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